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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/887,853 | 06/21/2001 | L. L. Houston | PP00926.106<br>2300-0926.05 | 9213 |

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| EXAMINER | |
|---|---|
| CANELLA, KAREN A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1643 | |

DATE MAILED: 09/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/887,853 | HOUSTON ET AL. | |
| | Examiner | Art Unit | |
| | Karen A. Canella | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) 77-86 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 77-85 is/are rejected.

7)☐ Claim(s) 86 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Please note that the examiner assignment for this application has changed.

2. Claims 77-86 are pending and under consideration.

3. Sections of Title 35, U.S. Code, not found in this action can be found in a prior action.

4. Claim 83 is objected to for being a duplicate of claim 80. Claim 84 and 85 also duplicate the subject matter of claims 81 and 82; Claim 86 is therefore objected to for being dependent on claim 84.

5. Claims 77-85 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2 and 22-24 of U.S. Patent No. 5,534,254 in view of Huston et al (WO 88/09344).

Claim 77 is drawn to an isolated protein comprising (a) a first polypeptide domain comprising CDR interposed between framework regions derived from human immunoglobulins and having the general formula FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4, and (b) a second polypeptide domain comprising CDRs interposed between framework regions derived from human immunoglobulins and having the general formula FR1'-CDR1'-FR2'-CDR2'-FR3'-CDR3'-FR4', wherein CDR1, CDR2, CDR3, CDR1', CDR2' and CDR3' are residues 31-35, 50-66, 99-104, 157-167, 183-189 and 222-240, respectively, of SEQ ID NO:6, and wherein said first and said second domains together are capable of forming a binding site for c-erbB2. Claim 78 embodies the protein of claim 77 wherein said first and second polypeptides are capable of forming a humanized antibody. Claim 79 embodies the protein of claim 78 wherein the FR sequences are from a human myeloma antibody. Claims 80 and 83 embody the protein of claim 77 wherein the first and second peptide domains are linked by a polypeptide linker. Claims 81 and 84 embody the protein of claim 80 and 83 wherein the polypeptide linker comprises at least 10 amino acids. Claims 82 and 8 embody the protein of claim 81 and 84 wherein the polypeptide linker comprises SEQ ID NO:7 [(Gly4Ser)3].

Claims 1 and 2 of the '254 patent are drawn to a composition comprising an sFv comprising two separate polypeptide chains, each of which have a an amino acid sequence comprising two polypeptide domains connected by a polypeptide linker sequence, the amino acid sequence of said domains comprising CDR regions interposed between frameworks regions, the framework regions and CDRs of each sFv defining a binding site for an antigen. Claim 22 embodies the compositions of claims 1 or 2 wherein the framework sequences are derived from a human antibody. Claim 23 embodies the compositions of claims 1 or 2 wherein said CDR sequences are derived from an immunoglobulin that binds to the c-erbB-2 antigen. Claim 24 embodies the composition of claim 23 wherein CDR sequences are derived from 520C9. The claims of the patent do not specify the amino acid sequences of the CDR regions derived from the 520C9 antibody, or the polypeptide linker sequence of SEQ ID NO:7.

Huston et al teach a method of making humanized antibodies (Legend for Figure 5 and page 23, lines 4-16) and single chain antibodies comprising the generalized formula FR1-X1-FR2-X2-FR3-X3-FR4- (page 43, lines 20-28), and the linker sequence, (Gly4Ser)3, for connecting two polypeptide domains which does not interfere with domain folding and has little propensity for secondary structure, but is short enough so that both polypeptides can interact (page 52, lines 10-23). Huston et al teach a construct comprising a master human immunoglobulin framework which may be used to insert any human CDR sequence (page 51, lines 4-8).

The instant claims are obvious over the claims of the '254 because claim 22 of the patent specifies human framework regions, and claims 23 and 24 require CDR regions derived from the 520C9 antibody, wherein said antibody binds to c-erbB-2. It would be obvious to one of skill in the art to sequence the polynucleotides encoding the 520C9 antibody and use the sequence information in the same way as Huston et al to express a sFv comprising the CDR of the heavy chain of 520C9 interspersed between human immunoglobulin framework regions, and a sFv comprising the CDR of the light chain of 520C9 interspersed between human immunoglobulin framework regions and join both sFv by the linker sequence (Gly4Ser)3. One of skill in the art would have been motivated to o so by the teachings of Huston et al on how to express sFv having human framework regions, and how to link to link two sFv comprising a heavy chain region to a sFv comprising a light chain region by means of the linker sequence (Gly4Ser)3

which held the two sFv at an appropriate distance for interaction to form an antigen-binding site, but which did not interfere in the secondary structure of the sFv.

6. All other rejections and objections as set forth in a previous Office action are withdrawn in light of applicant's arguments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
9/19/2005

KAREN A. CANELLA PH.D
PRIMARY EXAMINER